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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/068,460	02/06/2002	Roger Craig	18747/2012	8894
29933	7590	05/18/2004	EXAMINER	
PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199			PARAS JR, PETER	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

8/12

Office Action Summary

Application No.

10/068,460

Applicant(s)

CRAIG ET AL.

Examiner

Peter Paras, Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 15-20 and 22-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0603.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 1-26 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-14 in response received on 10/14/03 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden for the Examiner to search the claims of Groups I and II. This is not found persuasive because as set forth in the Restriction requirement inventions related as product and process of use can be shown as distinct is the product as claimed can be used in a materially different process of using that product (MPEP 806.05(h)). It is maintained the products of Group II can be used in materially different processes from the process of Group I. It is further maintained the vector of Group II can be used to transform insect cells in vitro to screen for potential insecticides and the transgenic insect of Group II can be used to produce a protein. Therefore, the restriction requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

It is noted that claim 21 was inadvertently placed in Group II. Since claim 21 depends from claim 1, directed to a method for controlling a population of target insects, it will be examined with elected Group I.

Claims 15-20 and 22-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response received on 10/14/03.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications filed in Great Britain on 8/6/99 and 8/7/00. It is noted, however, that applicant has not filed certified copies of the British applications as required by 35 U.S.C. 119(b).

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

In addition, the filing date of PCT/GB00/03043 as listed in the oath is incorrect. It appears the correct filing date should be 8/7/00.

Drawings

The drawings filed on 2/6/02 are approved.

Sequence Compliance

The sequence listings in paper and computer readable forms have been entered.
The instant application is now in compliance with the sequence rules.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to methods for controlling a population of target insects comprising transforming a plurality of target insects with a transgene encoding a constituent of an enzyme/prodrug system operably linked to a regulatory region is sex-specific and administering the remaining component of the system.

The specification discusses that the invention features a system for controlling target insect populations. See page 2. The specification discusses that the invention features a system comprising an enzyme/prodrug system under the control of a sex-specific promoter. See pages 2-6. The specification postulates that the enzyme component of the enzyme/prodrug system would be expressed in the desired sex of a target insect and would be capable of converting a prodrug into an active drug. Activated drugs would then be able to either sterilize or kill the desired sex of a target insect according to the discussions of the instant specification. While the specification contemplates that such an enzyme/prodrug system in conjunction with an insect sex-

specific promoter would be able to control a target insect population, the specification fails to provide any relevant teachings or specific guidance which enable the claimed methods of controlling a population of target insects. The claimed methods when taken with the guidance provided by the instant specification appear to be undeveloped and unpredictable at best. In view of the lack of guidance provided by the specification it would have required undue experimentation to use make and use the invention as claimed.

The claimed methods are unpredictable and undeveloped for controlling an insect population. The working examples provided by the specification (pages 18-21) discuss creation of transgenic *Drosophila* lines expressing a gene encoding cytosine deaminase (CD) operably linked to the Yp1 fat body promoter, a female-specific promoter. When expressed, CD is capable of converting non-toxic precursor 5-fluorocytosine (5-FC) into cytotoxic 5-fluorouracil (5-FU). In a laboratory setting female transgenic *Drosophila* were killed when treated with 5-FU. However, the goal of the instant invention according to the specification (see page 13) is to release transgenic insects into wild-type insect populations. The transgene is transmitted through breeding into a wild-type population to produce target populations of insects susceptible to a pro-drug or pro-insecticide.

The instant invention appears to be unpredictable and undeveloped in light of Markaki et al (*Insect Biochemistry and Molecular Biology*, 2004, 34: 131-137), which discusses the claimed invention and its limitations. Markaki et al suggest the CD/5-FC/Yp1 promoter system is unsuitable for large-scale applications due to delayed

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action, high cost of 5-FC, and observed sensitivity of non-transgenic males. Fly lethality was observed on only day 6 after exposure to 5-FC or 5-FU, wherein inefficient uptake of the analogues may be the cause of apparent delayed toxicity. Moreover, delayed action could also be attributed to the fact that adult flies consist mainly of post-mitotic, non-growing cells, which are thought to be less sensitive to 5-FU toxicity. Markaki et al also observe that for efficient genetic sexing schemes bioactivation should take place early in development. However, the YP1 promoter/enhancer directs expression only in the fat body of adult females. Also regulation of the YP1 promoter in certain insect species is diet-dependent. See page 135, columns 1-2. Markaki et al concludes by pointing to potential future success of enzyme/prodrug system in controlling target insect populations. See page 136. The instant specification has not provided working examples or guidance with respect to use of other promoters in accordance with the claimed invention.

In addition, with regard to use of promoters in conjunction with the enzyme/prodrug system of the claimed invention, the art suggests that sex-specific and conditional promoters are key components for developing transgenic sexing systems. See Komitopoulou et al (Insect Biochemistry and Molecular Biology, 2004, 34: 149-157). With respect to female-specific promoters, Komitopoulou et al observes that while a number of medfly female-specific genes have been cloned detailed functional analysis of their promoters and regulatory elements has not been conducted. See page 152, in column 2. With respect to conditional promoters, the hsp70 promoter potentially could be used for developing sexing systems. However, the hsp 70 promoter has relatively

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now activity in non-Drosophilid insects as compared to that in *Drosophila*. See page 153. Likewise, the actin 5C promoter, a constitutive promoter, has significantly lower activity in non-drosophilid species. See page 155. In light of the above, it appears that appropriate sex-specific and/or conditional promoters are not readily available beyond *Drosophila*. Komitopoulou et al, corroborates this point by concluding that “a number of promoters show different sex and tissue specificity as well as strength between *Drosophila* and other insect species suggesting that homologous components should be considered for developing transgenic sexing and marker systems in insect pests”. Given the teachings of the instant specification and the state of the art as represented by Komitopoulou it appears that promoters for use in the claimed methods are undeveloped at best, their activities being unpredictable across insect species.

Given the lack of guidance provided by the instant specification, and the unpredictable and undeveloped nature of the enzyme/prodrug/sex-specific promoter systems in insects, it would have required undue experimentation to make and use the invention as claimed.

Claims 1-14 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to methods for controlling a population of target insects comprising transforming a plurality of target insects with a transgene encoding a constituent of an enzyme/prodrug system operably linked to a regulatory region is sex-specific and administering the remaining component of the system.

The nucleotide sequences that comprise sex-specific insect regulatory regions encompassed within the genus, for use in the claimed methods, have not been disclosed. The specification has disclosed use of the Yp1 promoter (sequence not disclosed), which was derived from *Drosophila*, but has not disclosed any other promoters for use in the claimed methods. Based upon the prior art there is expected to be variation among the species of DNAs comprising insect sex-specific regulatory regions, as the DNA sequences would be expected to vary among insect species and corresponding genes. There is no evidence on the record of a relationship between the structures of any of the insect sex-specific regulatory regions that would provide any reliable information about the structure of regulatory regions within the genus. There is no evidence on the record that the Yp1 promoter had a known structural relationship to any other sex-specific insect regulatory region. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus of sex-specific insect regulatory regions, because the *Drosophila* Yp1 promoter is not representative of the claimed genus. Consequently, since Applicant was in possession of only the *Drosophila* Yp1 promoter and since the art recognized variation among the species of the genus of sex-specific insect regulatory regions, the *Drosophila* Yp1 promoter was

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not representative of the claimed genus. Therefore, Applicant was not in possession of the genus of DNA sequences of sex-specific insect regulatory regions as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Conclusion

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is (571) 272-0732. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Peter Paras, Jr.

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**PETER PARAS, JR.
PRIMARY EXAMINER**

A handwritten signature in cursive script that reads "Pete Paras".